AMERICAN Journal of Pharmacy

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

New Women's Residence Hall
Philadelphia College of Pharmacy & Science

Since 1825 *March 1958*

American Journal of Pharmacy

Published monthly by the Philadelphia College of Pharmacy and Science
43d Street, Kingsessing and Woodland Avenues, Philadelphia 4, Pa.

Annual Subscription $4.00 — Foreign Postage, 25 Cents Extra
Single Numbers, 40 Cents — Back Numbers, 50 Cents

Entered as Second-Class Matter March 27, 1937, at the Post Office at Philadelphia, Pa.
Under Act of March 3, 1879

NOW! for Angina Pectoris–

Remarkable New

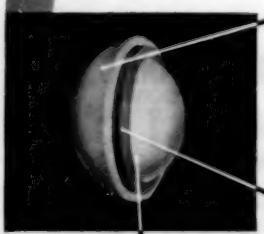
Dilcoron

TRADEMARK

Dual-Action Tablets

with *"FLAVOR-TIMER"*

Orally for Continuous Prophylaxis and Maintenance Therapy
Sublingually for Prompt Relief from Acute Anginal Attack



1. Outer jacket of DILCORON tablet contains quick acting glyceryl trinitrate (nitroglycerin)—0.4 mg. (1/150 grain). Tablet is held under tongue until citrus flavor disappears; provides rapid relief in acute or anticipated attack.

2. The middle layer of the tablet is the citrus "flavor-timer"; signals patient when to swallow.

3. The inner core contains long acting pentaerythritol tetranitrate—15 mg. (¼ grain). It is swallowed for slow enteric absorption and lasting protection.

Supplied in bottles of 100.

DILCORON TABLETS WILL BE ETHICALLY ADVERTISED AND DETAILED—HEAVILY PRESCRIBED!

BE READY! STOCK NOW.

Winthrop LABORATORIES
1450 Broadway, New York 18, N. Y.

PHARMACEUTICALS IN DAILY DEMAND
ETHICALLY ADVERTISED AND DETAILED

WHEN PATIENTS NEED HIGH POTENCY B-COMPLEX AND C

THERA-COMBEX® KAPSEALS®

Doctors recommend this established favorite to speed convalescence after operations or illness . . . to overcome specific vitamin deficiency states involving factors of the B-complex or vitamin C. Take a look at the formula and you'll see why.

Dependable vitamin therapy means dependable sales . . . so keep an eye on your THERA-COMBEX stock.

Each Kapseal contains:

Vitamin B_1 (thiamine) mononitrate	25 mg.
Vitamin B_2 (riboflavin)	15 mg.
Nicotinamide (niacinamide)	100 mg.
Folic acid	2.5 mg.
Vitamin B_6 (pyridoxine hydrochloride)	1 mg.
Vitamin B_{12} (crystalline)	5 mcg.
Pantothenic acid (as sodium salt)	10 mg.
Vitamin C (ascorbic acid)	150 mg.
Taka-Diastase®	2½ gr.

Bottles of 100 and 1,000 Kapseals.

PARKE, DAVIS & COMPANY · DETROIT 32, MICHIGAN

AMERICAN JOURNAL OF PHARMACY

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

Vol. 130 MARCH 1958 No. 3

CONTENTS

E D I T O R I A L

CONSERVATISM NOT HUCKSTERISM

THE extent to which overenthusiastic and unrestrained copy writers can embarrass both scientific workers and conservative pharmaceutical manufacturers was pointedly illustrated recently by a release, the language of which we shall not quote precisely. In this release, the suggestion was made that a new steroid substance having marked progestin activity offered a simple solution to Japan's overpopulation problem and that it was an effective oral contraceptive. It is true, of course, that a hurried telegram sought to correct this ill-advised and utterly ridiculous suggestion, and attempted to modify somewhat and to make more acceptable the language of the original release.

Unfortunately, the damage was already done since one can never effectively recall something of this sort. Some very distinguished steroid chemists were made to look rather foolish and, by implication, one of the pharmaceutical companies of very high reputation could not help but be greatly embarrassed even though they were completely lacking in responsibility for the release. The truth is that it was not even their agency which sent out this press release nor was it sent out in their behalf.

While we do not lay claim to an understanding of all of the profundities of copy writing for advertising and publicity purposes, it is difficult to understand how anyone with a reasonable degree of education and an appreciation of human beings and their interrelationships could be so presumptuous as to suggest that the staggering problem of overpopulation such as has been faced by Japan for several decades could be so readily solved. You can well imagine what the reaction of some of our friends in Japan would be if they were to read that we have it all mapped out for them and all they need to do is take our advice.

The concept of a potent steroid which will suppress ovulation serving as an oral contraceptive is just as unsound, although there may be some better excuse for such a suggestion coming from those who have no understanding of human physiology and the role of endocrine substances in the reproductive process. While we do not deny that overpopulation constitutes a serious economic problem in

many countries and that it can be a factor leading to aggression and an attempt to seize less highly populated land areas, a drug suppressing ovulation does not seem to be the solution to this problem. We are not questioning the use of such a drug in those cases where it is indicated by a competent medical examination since, with the suppression of ovulation, many other desirable therapeutic measures can be attained. By the same token, however, when used in a perfectly normal person, it is inconceivable that suppressing ovulation would not cause many highly undesirable side effects. For example, would it not be expected that, with such potent steroid therapy, pituitary function would be modified and, if it were, there might be no end of unpleasant and thoroughly undesirable long-range effects? These, of course, would be in addition to the effect on ovarian function itself which would surely be accompanied by undesirable effects if practiced over any long period of time.

The reason that we call attention to this incident is because it has been our impression for many years now that some advertising agencies often fail to recognize the necessity for a final review of all copy by some well-informed and scientifically trained staff member. While it may be perfectly all right to advertise soap and toothpaste in glowing terms completely devoid of all semblance of truth, this same philosophy must not be extended to the area of drug products. The drug industry has a very deep responsibility to the public and it dare not let the "Madison Avenue boys" sabotage the fine accomplishments which it has made, and which it is making, by ill-chosen and rashly conceived words. Those who in this instance were harmed by the over-exuberance of the copy writers have our sympathy and it is to those who are in a position to prevent any future repetition of this fiasco that we direct these words.

L. F. Tice

THE TURBIDOMETRIC DETERMINATION OF LYSOZYME IN ANIMAL GASTRIC JUICE *

By Morton E. Goldberg and G. Victor Rossi

THAT certain body tissues and secretions possess bacteriolytic and bacteriocidal properties has long been known. As stated by Salton (1), as early as the beginning of this century, some investigators had considered the possibility that bacteriolytic substances may possess properties in common with enzymes. In 1922 Fleming (2) discovered one such substance capable of lysing suspensions of certain bacteria. He termed this substance "lysozyme". At the same time, Fleming also was successful in isolating a gram positive coccus which he named Micrococcus lysodeikticus. This organism was demonstrated to be the most susceptible organism to the lytic action of lysozyme. Fleming (2, 3) and others (4, 5) have detected lysozyme in tears, saliva, nasal mucus, serum, cartilage, plasma, gastric juice and other tissues and body secretions. However, the richest source of the enzyme is egg white (2). Since its isolation (6) and crystallization (7), lysozyme obtained from egg white has become a provisional standard for the assay of lysozyme in tissues and secretions.

Lysozyme is a protein of comparatively low molecular weight. Various investigators have determined this molecular weight to be approximately 14,000 to 17,000 (8, 9, 10). Lysozyme has an isoelectric point at pH 10.5-11 (8) and is most stable in solution at pH 6.0-6.5 (11). It is stable to heat and weakly acidic solutions (11) but in the presence of pepsin it is readily deactivated (12). Accurate quantitative determination of the enzyme in gastric juice, therefore, depends upon immediate adjustment of the gastric sample to pH 6.0-6.5, since below this pH pepsin immediately begins to bind and inactivate the lysozyme. At pH 7 or above (13) enzymatic decomposition occurs with extreme rapidity.

Enzymes possessing lysozyme activity have been isolated from plant sources, however these enzymes have been found to be chemically quite different from the lysozyme derived from egg white (14). The

* Received from the LaWall Memorial Laboratory of Pharmacology and Biochemistry, Philadelphia College of Pharmacy and Science, Philadelphia 4, Penna.

enzyme employed in this study [1] was prepared according to the procedure of Alderton and Fevold (7).

Certain investigators (15, 16) have related abnormal levels of lysozyme to several pathological disorders of the gastrointestinal tract including peptic ulceration and ulcerative colitis. In an investigation currently being conducted in the LaWall Memorial Laboratory of Pharmacology and Biochemistry, it has become necessary to develop an accurate method for the determination of lysozyme activity in animal gastric juice. This investigation, which is part of a correlated study into the biochemistry of gastric juice in normal and ulcerated animals, will form the basis of a subsequent report.

Method

Two basic methods are currently employed in the determination of lysozyme activity. The enzyme may be determined by a viscosimetric procedure (17) or by a turbidometric procedure (18). In the method being described, we have used a modification of the bacteriolytic turbidometric procedure of Smolelis and Hartsell (19) and Lobstein and Fogelson (20). The theoretical basis for the procedure involves the fact that lysozyme will lyse, and thus reduce the turbidity of, a suspension of Micrococcus lysodeikticus under the prevailing conditions of the experiment. The concentration of lysozyme present in a solution may therefore be correlated with the transmittance.

The technique for obtaining animal gastric juice has been described previously (21). An aliquot of the gastric juice is adjusted to pH 6.0 with 0.25N sodium hydroxide and the sample is diluted to a suitable volume (to make a final concentration of 1:10) with phosphate buffer of pH 6.2.[2] Five ml. of this dilution are added to a test tube containing 5 ml. of a substrate prepared by uniformly suspending 60 mg. of killed Micrococcus lysodeikticus cells [3] in 100 ml. of phosphate buffer. The tube is inverted twice and allowed to stand at room temperature for exactly 60 minutes. At the end of this period, the tube is again inverted, the contents placed into a suitable cuvette, and the optical density read immediately in a Coleman

[1] Kindly supplied by Armour Laboratories, Chicago, Illinois.

[2] Bacto Lysozyme Buffer, Difco Laboratories, Detroit, Michigan.

[3] Bacto Lysozyme Substrate, Difco Laboratories, Detroit, Michigan.

Spectrophotometer, Model 14, set at 540 millimicrons. The instrument is adjusted to zero using a matched cuvette containing phosphate buffer. Since turbidity is also contributed by gastric juice itself, an additional aliquot of gastric juice of the corresponding dilution is also read in the spectrophotometer at the same wave-length noted. The optical density of the "blank" is subtracted from the optical density of the "test" solution. The resultant figure, representing the decrease in turbidity due to lysozyme activity is compared to a standard curve which is prepared as follows: A series of dilutions are prepared which contain crystalline egg white lysozyme in concentrations ranging from 0 to 1.5 mcg. in each 5.0 ml. of phosphate buffer. Each of these standard lysozyme solutions is transferred to a test tube containing 5.0 ml. of substrate suspension, inverted twice and allowed to react at room temperature for 60 minutes. At the end of this period, the solutions are read in the spectrophotometer as previously described. A standard curve is prepared by plotting the concentration of lysozyme in tenths of a microgram against the optical density obtained at 540 millimicrons. A straight line has always been obtained. The test samples are compared to the standard curve and results are expressed as "micrograms of lysozyme activity equivalent to crystalline egg white lysozyme per milliliter of gastric juice". Depending upon the commercial batch of substrate employed and the temperature of the experiment, the standard curve will vary slightly from day to day, however, results obtained on any given day with the same substrate are reproducible. For this reason, the standard curve is repeated with each group of determinations.

Results obtained in several hundred analyses, using the method described in this report, indicate the limits of accuracy of the method to be $\pm$ 5%.

REFERENCES

(1) Salton, M. R. J., *Bacteriol. Rev., 21,* 82 (1957).

(2) Fleming, A., *Proc. Roy. Soc.* (London), *93,* 306 (1922).

(3) Fleming, A., *Proc. Roy. Soc. Med., 26,* 71 (1932).

(4) Gray, S. J., Reifenstein, R. W., Young, J. C. G., Spiro, H. M. and Connolly, E. P., *J. Clin. Invest., 29,* 1595 (1950).

(5) Prudden, J. F. and Lane, N., *Gastroenterology, 15,* 104 (1950).

(6) Alderton, G., Ward, W. H. and Fevold, L. H., *J. Biol. Chem., 157,* 43 (1945).

(7) Alderton, G. and Fevold, L. H., *ibid., 164,* 1 (1946).

(8) McMeekin, T. L. and Warner, R. C., *Ann. Rev. Biochem., 15,* 119 (1946).

(9) Palmer, K. J., Ballantyne, M. and Galvin, J. A., *J. Am. Chem. Soc., 70,* 906 (1948).

(10) Fevold, L. H., *Advances in Protein Chem., 6,* 187 (1951).

(11) Meyer, K., Thompson, R. and Khorazo, D., *J. Biol. Chem., 113,* 303 (1936).

(12) Caputo, A., *Experientia, Basel, 11,* 401 (1955).

(13) Greenberg, D. M., *J. Biol. Chem., 82,* 545 (1929).

(14) Smith, E. L., Kimmel, J. R., Brown, D. M. and Thompson, E. O. P., *ibid., 215,* 67 (1955).

(15) Meyer, K., Prudden, J. F., Lehman, W. L. and Steinberg, A., *Proc. Soc. Exp. Biol. Med., 65,* 220 (1947).

(16) Nickel, W. F., Jr., Gordon, C. M. and Andrus, W. D., *Gastroenteroloy, 17,* 406 (1951).

(17) Meyer, K. and Hahnel, E., *J. Biol. Chem., 163,* 723 (1946).

(18) Boasson, E. H., *J. Immunol., 34,* 281 (1938).

(19) Smolelis, A. N. and Hartsell, S. E., *J. Bacteriol., 58,* 731 (1949).

(20) Lobstein, O. E. and Fogelson, S. J., *Quart. Bull. Northwestern Univ. Med. School, 25,* 89 (1951).

(21) Goldberg, M. E. and Rossi, G. V., *Am. J. Pharm., 128,* 263 (1956).

STERILIZATION OF COLLOIDAL OATMEAL FOR USE AS A DUSTING POWDER IN SURGICAL GLOVES *

By Albert M. White and Louis P. Jeffrey **

Introduction

THE value of colloidal oatmeal in the preparation of colloid baths, has been reported in the literature (1) as constituting an essential part of the external treatment for acute and chronic dermatoses. A colloidal bath is prepared by using one cupful of powdered colloidal oatmeal to a tub of lukewarm water. Dr. Melvin Grais in his article (2) reports that the buffer action of colloidal oatmeal produced an immediate and sustained pH comparable to that of normal skin, even after the skin was alkali-treated. On the basis of viscosimetric measurements, the tenacity of the colloidal oatmeal skin coating is of such nature as to counteract the alkalinity of tissue exudate as well as the eroding action of clothing on the protective demulcent film. In his conclusions, Dr. Grais states, that the cleansing of soap-sensitive or irritated skin with colloidal oatmeal, proved very effective. Colloidal oatmeal exhibited a remarkable lack of skin sensitizing and irritating properties.

Colloidal oatmeal is recommended to be used as an agent to overcome hand eczema as the result of wearing rubber gloves. Dr. Becker's investigations (3), found that a coating of colloidal oatmeal protected sensitive hands against the irritation of rubber gloves. No allergic reactions were encountered during this therapy.

From these reports and findings, the use of colloidal oatmeal as a suitable dusting powder for surgical rubber gloves, was believed to have real merit. A desirable method for the sterilization of this powder was needed however, before it could be used for this purpose.

---

* Presented at the Fourth Pan-American Congress of Pharmacy and Biochemistry, Washington, D. C., November, 1957.

** Albert M. White, M. S., Assistant Professor in Pharmacy, Albany College of Pharmacy, Union University, Albany, New York. Louis P. Jeffrey, M. S., Pharmacist-in-Chief, Department of Pharmacy, Albany Hospital, Albany, N. Y. Product conducted in the Research and Control Laboratory, Department of Pharmacy, Albany Hospital, Albany, New York.

Experimental

Colloidal Oatmeal [1] is a concentrate of the gum fraction of the oat grain. It contains approximately 20% protein.

The colloidal oatmeal used in this experiment was put in small polyethylene packets and larger paper bags. The sterilization of colloidal oatmeal, using either an Autoclave or a Hot Air Oven, was then carried out with the following results. The powder was first sterilized in an autoclave at 121° C. and 15 pounds pressure. The exposure time—seven, ten and fifteen minutes—produced the same results. In each instance, generally, the powder clumped and hardened. Some paper bags split open, while the polyethylene packets showed no splitting.

The next attempt at sterilization was with a hot air oven. Sterilization at 160°, again varying the exposure time,—seven, ten and fifteen minutes—had the following results. The packages were scorched and the powder changed from a white to a brown color. This occurred with both the large paper and smaller polyethylene packages. The results of sterilization with a Hot Air Oven was proven to be unsatisfactory.

A further investigation of sterilization by Autoclave at 121° C. for 15 minutes was then undertaken. The following four procedures using a sterilizing pack were carried out.

1. Small polyethylene packets were taped on the outside of the pack to be sterilized.
2. Small polyethylene packets were taped on the outside of the envelope.
3. Small polyethylene packets were taped on the inside of the envelope.
4. Small polyethylene packets were placed in surgical rubber gloves and enveloped.

In each step the assembled unit was autoclaved for 121° C. for 15 minutes and after autoclaving, the sterilized sealed colloidal oatmeal packet was pressed with the fingers several times.

The best results were obtained with the fourth step. The product had very little clumping and hardening, thus resulting in a free-flowing

1. The colloidal oatmeal used in the study was supplied by the Aveeno Corporation, 250 West 47th Street, New York 19, New York.

powder. This technique appeared to be the most desirable in the practical use of colloidal oatmeal as a dusting powder in surgical rubber gloves. All other procedures, resulted in a great deal of clumped material which would not lend itself readily to the dusting of gloves. Samples of the various procedures were tested for sterility. All the material that was sterilized for 15 minutes at 121° in an autoclave, exhibited no growth of bacteria. The laboratory (4) used Brewer's Thioglycolate and Sadrow's Broth as the culture media, incubating for ten days at 37° C.

Finally, this procedure was carried out using colloidal oatmeal contaminated with *Bacillus subtilis*. One ml. of a 24 hour Broth Culture of *Bacillus subtilis* was injected into an 18 oz. carton of colloidal oatmeal (5). The contaminated colloidal oatmeal was then packaged in large paper bags. The procedure as outlined in the fourth step produced a suitable dusting product. It was free-flowing, with no clumping or hardening of the colloidal oatmeal. The results of sterility tests indicated that there was no growth of bacteria. A paper bag that was not subjected to this sterilization procedure, resulted in the isolation of *Bacillus subtilis*.

Conclusion

1. The use of colloidal oatmeal as a dusting powder for surgical gloves, depends upon a suitable sterilization procedure since the gloves after being dusted must be maintained in a sterile condition.

2. Sterilization by Hot Air Oven and Autoclave were experimented with using colloidal oatmeal powder. Both procedures resulted in a product not suitable for dusting.

3. Further investigation of sterilization by Autoclave using a sterilizing pack, was undertaken. The majority of procedures used resulted in an unsatisfactory product.

4. The best results were obtained by placing small polyethylene packets of colloidal oatmeal in surgical rubber gloves, enveloped and autoclaved at 121° C., for 15 minutes.

5. Bacteriological tests on contaminated and non-contaminated colloidal oatmeal packages using the Autoclave procedure, proved it to be the proper sterilizing procedure.

Summary

From the results of these experiments, the best procedure for the sterilization of Colloidal oatmeal as a dusting powder appears to be in small polyethylene packets placed in surgical rubber gloves and enveloped. These packs are then sterilized in an autoclave at 121° C. for 15 minutes. Before opening the colloidal oatmeal package, the powder is pressed several times with the fingers. Then, proceed to dust the gloves.

REFERENCES

(1) Kierland, R. R. and Ede, M., *A. M. A. Arch. Dermat. & Syph. 63,* 4, 602 (1951).

(2) Grais, M., M. D., *A. M. A. Arch. Dermat. & Syph. 68,* 402-407 (1953).

(3) Becker, S. William, *A. M. A. Arch. Dermat. & Syph. 71,* 378 (1955).

(4) Wright, Arthur W., M. D., Bacteriology Laboratory, Albany Medical College, Union University, Albany, New York.

(5) Binkley, Lowell E., A. M., Assistant Professor, Bacteriology Department, Albany College of Pharmacy, Union University, Albany, New York.

STUDIES OF THE GENUS THYMUS

PART III

Comparison of the Diagnostic Microscopical Characteristics of Thymus Chamaedrys Fries and Thymus Herba-barona Loisel

By Ikram Hassan * and M. S. Dunn **

IN a recently published paper (1), the authors have made microscopical studies of Thymus vulgaris Linn. and Thymus Serpyllum Linn. The present paper reports microscopical studies made on Thymus Chamaedrys Fries, and Thymus Herba-barona Loisel. Tissue elements of these two species were studied from the leaves, stems and flowering tops.

Nine samples of Thymus Chamaedrys Fries and eight samples of Thymus Herba-barona Loisel were studied from the following authoritative sources: Herbaria of the University of West Virginia. Philadelphia Academy of Natural Sciences, Botanical Garden of the University of Montreal, Harvard University; United States National Herbarium; Martindale Collection of the Philadelphia College of Pharmacy and Science; the Herbarium of the New York Botanical Garden; and the Bailey Hortorium. In each case, a small branch containing a few leaves and a few flowers were carefully detached and placed in a paper envelop and all pertinent information of collector and identifier written on the face of the envelop.

Although the materials used in these studies were obtained from the herbarium sheets which were either collected or identified by recognized plant taxonomists, still the identity of each sample was checked by comparison with descriptions given by Bailey (3), Hegi (4), and Ronneger (5).

---

* Instructor, Department of Biology, Philadelphia College of Pharmacy and Science, Philadelphia, Pa. In partial fulfillment of the requirements for the Degree of Doctor of Science in Biology.

** Professor of Biology and Director of the Biology Department, Philadelphia College of Pharmacy and Science, Philadelphia, Pa.

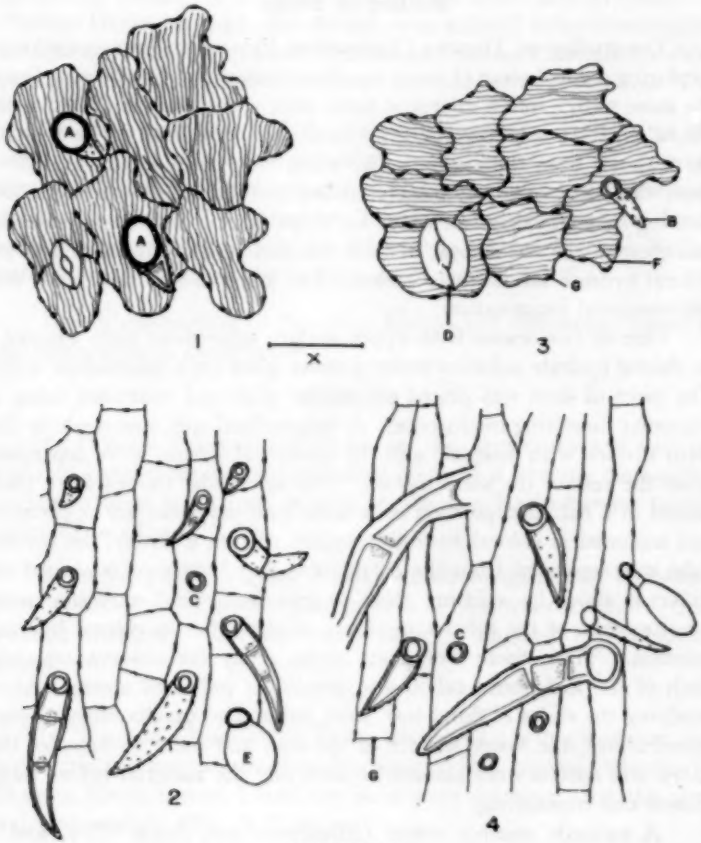


FIGURE I.

THYMUS CHAMAEDRYS FRIES.

1. Upper Epidermis of Leaf.
2. Epidermis of the Stem Showing Rows of Trichomes.

THYMUS HERBA-BARONA LOISEL.

3. Upper Epidermis of Leaf.
4. Epidermis of the Stem (Showing Trichomes Scattered over the Surface).

A—Unicellular Nonglandular (Papilla-Like) Trichomes. B—Unicellular Nonglandular Longer Trichome. C—Nonglandular Trichome Scars. D—Stomata. E—Glandular Hair. F—Cuticular Striations. G—Beaded Wall of Epidermal Cell.

All drawings made with the aid of the camera lucida. Scale X for all figures = 34 microns.

Method of Study

The studies on Thymus Chamaedrys Fries were first carried out by placing a small piece of stem, two floral leaves and two flowers from the same source into a microtest tube, which was then half filled with chloral hydrate solution (50 gms. in 20 cc. of water). The rest of the material from the source under study was saved for future reference. The test tube was loosely corked and either left overnight for clearing or warmed in hot water for a few hours. After the material had cleared, the old chloral hydrate solution was discarded and fresh chloral hydrate solution was added. The material was now ready for microscopical examination.

One or two leaves with upper surface uppermost were mounted in chloral hydrate solution under a cover glass on a microscope slide. The piece of stem was placed on another slide and examined using a binocular dissecting microscope. A longitudinal split was made in the stem surface with a needle and the epidermal tissues were separated from the rest of the stem tissues. The epidermal tissues were then placed in a flattened position on a slide with outer surface uppermost and mounted in chloral hydrate solution. From a flower, the corolla tube was separated from the calyx tube, and both were mounted on different slides by splitting them longitudinally and mounting with inner surface of the tubes uppermost on the slides in chloral hydrate solution. Thus, there were four slides ready for observation—one each of the leaf, stem, calyx, and corolla as indicated above. After studying the slides of floral leaf, stem, calyx, and carolla tubes as prepared above, the lower surface of the leaf, and outer surfaces of the calyx and corolla were studied by inverting the material before mentioned and remounting.

A palisade number count (Silverman and Dunn (2)), and a count of leaf stomata per small central square unit of the Howard micrometer ruling was also made in a number of cases.

Summary

On the basis of our detailed tabulated data which is not published in this article, but which can be obtained by those interested from the authors, the following summary is given of our findings:

I. The comparison of the palisade numbers of Thymus Chamaedrys Fries and Thymus Herba-barona Loisel based upon the aver-

ages of 32 counts for Thymus Chamaedrys Fries and 24 counts of Thymus Herba-barona Loisel did not seem to be of value in separation of these species. The palisade number of Thymus Chamaedrys Fries averaged 12.1 while that of Thymus Herba-barona Loisel was 10.5.

II. The comparison of the average number of stomata of the lower epidermis of the leaf per small central square of the Howard micrometer ruling offered promise of being of value in distinguishing the two species. The value for Thymus Chamaedrys Fries based on the average of 32 counts was 22.5 while that of Thymus Herba-barona Loisel based on the average of 24 counts was 8.4.

III. A comparison of the other histological differences found in the two species is given below:

A. Floral Leaf

1. Thymus Chamaedrys Fries on the upper surface had invariably 1-celled papilla-like trichomes up to 55 μ whereas the 1-celled trichomes were fairly long in case of Thymus Herba-barona Loisel, up to 105 μ (Fig. I. 1, 3).

2. In the petiole region, 2 and 3-celled nonglandular trichomes were common in Thymus Chamaedrys Fries whereas more than 1-celled trichomes were extremely rare in Thymus Herba-barona Loisel.

B. Stem

In Thymus Chamaedrys Fries, trichomes (both glandular and nonglandular) were confined to four longitudinal regions, whereas in Thymus Herba-barona Loisel the hairs were scattered over the general stem surface (Fig. I. 2, 4).

C. Calyx

1. In Thymus Chamaedrys Fries as well as in Thymus Herba-barona Loisel, the outer epidermis of the tubular region of the calyx, in the interrib region, showed cells with papillae fluted or ridged due to continuation of general epidermal cuticular striations (Fig. II. 1, 6). These cells in Thymus Chamaedrys Fries were found in the interrib spaces of the entire tube, whereas in Thymus Herba-barona Loisel they were only found below the bifid lip in the regions between the ribs. They were not found in the divided regions of either species.

2. In Thymus Chamaedrys Fries, the three broader sepals possessed 1-3 celled nonglandular marginal trichomes while the two narrower sepals had 1-4 celled nonglandular marginal trichomes. In Thymus Herba-barona Loisel, the three broader sepals showed mostly 1-celled nonglandular marginal trichomes while the narrower sepals had generally 2-celled or more than 2-celled nonglandular marginal trichomes (Fig. II. 5A, 5B, 7A, 7B).

3. In Thymus Chamaedrys Fries, 1-celled hairs with swollen upper ends were found in the interrib region of the outer surface whereas in Thymus Herba-barona Loisel, this trichome type was absent (Fig. II. 2).

D. Corolla

In the case of Thymus Chamaedrys Fries, clavate trichomes were situated as outgrowths of the free walls of the inner epidermis of the tubular part of the corolla below the trifid lip, whereas such trichomes were scattered over the inner surface of both lips and almost to the base of the corolla tube in Thymus Herba-barona Loisel (Fig. II. 3).

FIGURE II.

Thymus Chamaedrys Fries.

1. Outer Epidermis of the Calyx Tube, Interrib Region Showing Fluted or ridged Papillate Cells and Cuticular Striations.

2. One-Celled Glandular Hairs from Outer Surface of Calyx Showing Point of Attachment.

3. Clavate Unicellular Nonglandular Hairs from the Inner Surface of Corolla Tube Showing Centrifugal Projections.

4. Epidermis of the Divided Region of Calyx Showing Glandular Hair and Cuticular Striations.

5A. Broader Sepal Showing 1-3 Celled Nonglandular Marginal Trichomes.

5B. Narrower Sepal Showing 1-4 Celled Nonglandular Marginal Trichomes.

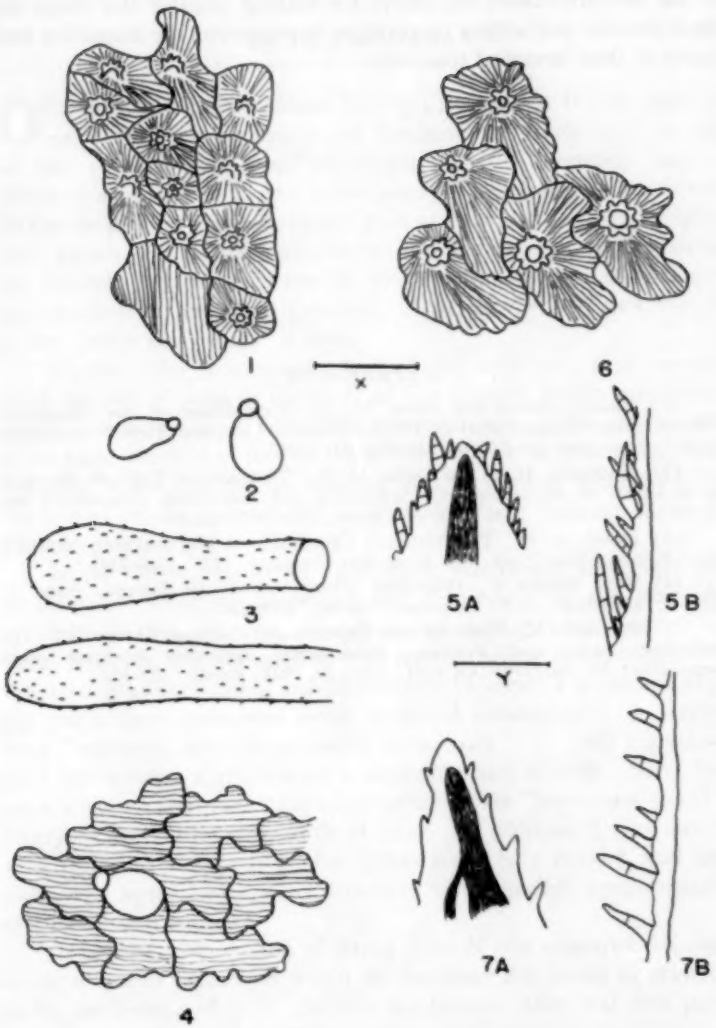
Thymus Herba-barona Loisel.

6. Outer Epidermis of the Calyx Tube Between the Ribs Showing Fluted or Ridged Papillate Cells and Cuticular Striations.

7A. Broader Sepal Showing 1-Celled Nonglandular Marginal Trichomes.

7B. Narrower Sepal Showing 1-2 Celled Nonglandular Marginal Trichomes.

All drawings made with the aid of the camera lucida. Scale X-34 microns for drawings 1-4, 6. Scale Y-150 microns for drawings 5A, 5B, 7A, 7B.


1
x
6
2
3
5A
5B
Y
4
7A
7B

The authors wish to express their deepest thanks to the curators of the herbaria mentioned above for making possible this study by their cheerful and willing cooperation in permitting the inspection and study of their botanical treasures.

REFERENCES

(1) Hassan, Ikram and Dunn, M. S., "Comparison of the Diagnostic Microscopical Characteristics of Thymus vulgaris Linn. and Thymus Serpyllum Linn." *Am. Jour. of Pharm. 129:*362-371 (1957).

(2) Silverman, H. I. and Dunn, M. S., "Comparative Palisade Numbers as a Means of Microscopically Separating and Identifying Peppermint and Spearmint Leaves." *Am. Jour. of Pharm. 128:*19-23 (1956).

(3) Bailey, L. H., The Standard Cyclopedia of Horticulture; Vol. VI, New Edition; New York The Macmillan Company, 1922; 3340-3342.

(4) Hegi, Gustav P., Illustrierte Flora Von Mittle Europa; Band V, Tiel 4; Munchen; J. F. Lehmanns Verlag; 2306-2327.

(5) Ronniger, K., "Beitrage zur Kenntnis der Gattung Thymus 1." Die britischen Arten Und Formen; Repertorium specierum novarum regni vegetabilis; Nr. 561/576; XX 6-21; Okt. 20, 1924; Berlin; 321-332.

ALDOUS HUXLEY AND TRANQUILIZERS

By Paul A. Doyle *

OF all his many books, Aldous Huxley's *Brave New World* seems to enjoy the most popularity and timelessness. Certainly, it is one of the greatest and most significant twentieth century novels. Huxley's satirical picture of a future world in which science has solved all human problems is sardonically grim and stirring and, yet, delightfully amusing. The stern totalitarianism, the scientific caste system, the test-tube babies, and even the electro-magnetic golf courses are unforgettable in their stark vividness. Also unforgettable as a feature of the "brave new world" is soma.

Huxley, who is immensely learned and well-read, first encountered the idea of soma in his study of Far Eastern Indian mysticism. In the lore of the East, soma had two meanings. First, it was one of the most powerful of the old Vedic deities, a sort of Hindu Bacchus. Secondly, soma also had the meaning of a mysterious drink made by the Indian priests and drunk by the Brahmins as well as offered as libations to their gods.

In the "brave new world", something was needed to prevent the people from becoming depressed and despondent by the manifold problems in life. At first, morphine and cocaine were used. The State, however, was not satisfied with these drugs, so it subsidized two thousand pharmacologists and biochemists to create a superior drug. Six years later, soma was being produced commercially—a perfect drug: "euphoric, narcotic, pleasantly hallucinant . . . half a gramme for a half-holiday, a gramme for a weekend," and so forth. Soma became a sort of pharmaceutical *vade mecum* in the "brave new world." Everyone carried his own bottle of soma. In addition, it was served with coffee in restaurants. Ice cream soma bars existed, and the police riot squad had a soma vaporizer which quelled pandemonium and restored tranquility.

When the 1946 edition of *Brave New World* appeared, Huxley wrote a special preface in which he discussed the future in relation to his predictions of 1932, the year his famous satire was first pub-

* Assistant Professor, Fordham University, College of Pharmacy.

lished. As a man with a vast scientific background who follows the developments of science closely, Dr. Huxley hinted that, perhaps, his prediction of soma was not so farfetched after all.

In 1954, Huxley published a book called *The Doors of Perception*. This treatise was a true story of the effects of mescalin. At the beginning of this book, Huxley traced much of the scholarly material on this drug. This material really originated in 1886 when the German pharmacologist, Ludwig Lewin, published the first systematic study of the cactus. Mescalin, however, had been known and used for centuries by the Indians of Mexico and the American Southwest as a stimulant and antispasmodic. Since the work of Lewin, mescalin research has been going on sporadically. Chemists have learned how to synthesize the drug; consequently, the supply no longer depends on the meager crop of desert cactus. Neurologists, physiologists, and psychologists have also studied the drug and its effects. Recently, it has been observed that there is a close similarity between mescalin and adrenalin in chemical composition. Also, it was discovered that adrenochrome, which is a product of the decomposition of adrenalin, can produce many symptoms characteristic of mescalin. The complete and exact relationship between adrenalin and mescalin is being probed still further.

One of the scientific investigators of mescalin asked Dr. Huxley to serve as a human guinea pig. Thus, in May, 1953, Huxley "swallowed four-tenths of a gram of mescalin dissolved in half a glass of water and sat down to wait for the results."

As is well-known, the brain is equipped with enzymes, some of which regulate the supply of glucose to the brain cells. Mescalin appears to inhibit the production of these enzymes and, hence, it lowers the amount of glucose available. As a result, although the intellect remains unimpaired, the will undergoes a lethargic paralyzation. The mescalin-taker has no desire to act. He wishes to think, to contemplate. He has no interest in human relations and necessary duties. Apparently, though, mescalin has no derogatory effect on the average individual. The "reasonably healthy person knows in advance that, so far as he is concerned, mescalin is completely innocuous, that its effects will pass off after eight or ten hours, leaving no hangover and consequently no craving for a renewal of the dose."

In *The Doors of Perception*, Huxley describes mescalin's effect on him. In all but one way—which need not be treated here—his reaction to the drug was similar to that of others who have taken it

to assist scientific research. Huxley's perception of vividly brilliant colors, his perception of the significance of contemplation, and other effects under the influence of mescalin make fascinating reading—but his conclusion is of more immediate interest for our purposes.

Suppose, suggests Huxley, a drug on the order of mescalin could be developed which could be used to relieve and cure alcoholism, the misuse of drugs, and other diseases and habits of a similar nature. In fact, this harmless drug might be a safe substitute for excesses which are severely injurious to mankind. We may well contemplate at some length the implications of this point. Mescalin is not the ideal drug for this purpose because: (1) it causes some people to have unpleasant visions and thoughts, and (2) its effects last from eight to ten hours, which for some people would be an inconveniently long time. But, as Huxley concludes, it is conceivable—not a certitude—that chemists and neurologists and pharmacologists may in time discover the ideal drug.

In two lectures delivered in New York City this year—one at the Manhattan Poetry Center, the other at the New York Academy of Sciences—and, slightly in his book *Heaven and Hell,* Dr. Huxley has enlarged upon the conclusion of *The Doors of Perception.* He feels that tranquilizers, now among commonly prescribed drugs, will be more revolutionary than achievements in nuclear physics. Obviously, of course, much research must be done on tranquilizers in the future but considerable investigation is already underway. Two items may be noted of many which could be cited in this connection.

We have all read of the successful use of tranquilizers for some patients in mental hospitals. In a recent Public Health Service monograph, Dr. Morton Kramer, chief of the biometrics branch, National Institute of Mental Health, noted that the drugs chlorpromazine and reserpine were significant because of their ability to reduce motor activity, disturbed behavior, tension, and anxiety without producing sleep. Yet, some adverse effects are known to result from certain tranquilizers; for example, automobile driving skills are unfavorably affected by meprobamate. Determining the safety of these behavior drugs presents scientific research with a vital and extremely important task.

Since heart weakness and disease are so rampant in modern life, any drug which could aid or alleviate this common bane would be an outstanding contribution to national health. Tests have already been begun to determine if certain drugs can control high blood pressure, prevent heart attacks, hardening of the arteries, and strokes. Among

the drugs now being studied and tested in this connection is the tranquilizer, reserpine.

In the near future, the pharmacy curriculum will be lengthened to a total of five years. This step is being taken, in part, to broaden the background and increase the knowledge of the pharmacy student. We, as educators of prospective pharmacists, must always attempt to correlate the relationship between the profession of pharmacy and life in its many phases and aspects. We must present pharmacy to the student not just from the retail point of view, but from its impact on health, research, and long-range thinking. Pharmacy is not parochial; it is universal and the student should be taught to think of it in its far-reaching and total aspects. Pharmacy needs students, teachers, and practitioners of vision. It must be aware of allied phases of thinking and knowledge. The Aldous Huxley popularization of and experiment in tranquilizers is an illustration to the point. In an age which has seen the development of drugs which we correctly label "miracle" and "wonder", Huxley's ideas have considerable importance and are not without logic. In 1932, soma in the "brave new world" was a fanciful, satiric suggestion but, in the future atomic world, soma may become a worth-while, salutary reality.

THE DAWN OF AMERICAN-MADE SYNTHETIC DRUGS *

By Aaron Lichtin [1] and Ira Leo Schamberg [2]

IT is a well accepted fact that an adequate supply of effective medicinal agents is an exceedingly important weapon in the fight against disease and the maintenance of good health. The nation which possesses the best equipped laboratories and the best trained personnel to operate them is surely bound to have the better chance to come out the victor in a struggle with disease. While this thinking is now generally established in this country, it took a world catastrophe, namely World War I to drive the idea home and ultimately give this Nation the preeminence which it enjoys in the field of drug and chemical manufacture. Up until that time, the United States was pretty well content to depend on European countries, particularly Germany, for its needs in this field.

Of 592 drugs listed in the 1916 edition of New and Nonofficial Remedies (1), 228 were imported into the United States from Germany. Among these were such important products as Aspirin, Anesthesine (benzocaine), Salvarsan (arsphenamine), Neosalvarsan (neoarsphenamine) Veronal (barbital) and Novocaine (procaine). The supply from Germany, the only source of many of these was abruptly cut off by World War I.

Not only was this country dependent on German imports for many valuable drugs, but it was also content to send its young scientists abroad for special graduate study. Facilities for such study were meager and poorly organized. It was not until after the War that, moved by a desire to stimulate interest in scientific and industrial chemistry at home, the Chemical Foundation, Inc., a quasi-govern-

---

* Read before the Section on Historical Pharmacy and Historical Biochemistry, Fourth Pan-American Congress of Pharmacy and Biochemistry, Washington, D. C., November 6th, 1957.

[1] Lecturer in Materia Medica and Drug Therapeutics, Graduate School of Medicine, University of Pennsylvania; Director Torch Laboratories, Philadelphia, Pa.

[2] Assistant Professor of Dermatology, Graduate School of Medicine, University of Pennsylvania; Senior Attending Dermatologist, Albert Einstein Medical Center, Northern Division.

mental agency released a report in 1921, entitled, "The Future and Progress of American Medicine in the Age of Chemistry." It summarized existing facilities for chemical research in medicine both at home and abroad and offered suggestions for further development. The report stated (2): "While there are in the United States a number of institutes and foundations for medical research doing most valuable work, there is none in which the problems are being approached primarily from the chemical standpoint. Consequently, few new lines of chemical investigation in relation to disease have been developed in this country and we have been largely dependent upon foreign countries, especially Germany, for discoveries relating to the applications of chemistry to disease. The Dermatological Research Laboratories of the Philadelphia Polyclinic have done very important work on the preparation of arsphenamine and on chemotherapeutic studies with this and other arsenic and also mercury compounds, as well as on metabolism in certain skin diseases."

The Dermatological Research Laboratories of the Philadelphia (3) Polyclinic and College for Graduates in Medicine, to mention the full name of the institute, was founded by Jay Frank Schamberg, M. D. in April, 1912, and were financially supported for several years by a Philadelphia philanthropist, P. A. B. Widener. As the title indicated, the initial sponsorship was given by the Philadelphia Polyclinic, now the Graduate Hospital of the University of Pennsylvania. The initial directors of the laboratories were Jay Frank Schamberg, M. D., Director, George W. Raiziss, Ph. D., Director of Chemistry, and John W. Kolmer, M. D. Director of Pathology. The first project undertaken was a comprehensive study of the physiological chemistry of psoriasis (4) (1913). During the following two years, the activities of the Laboratories were devoted chiefly to the investigation of chemotherapeutic agents, particularly organic mercurial and arsenical compounds (5). In retrospect, these accomplishments may be looked upon as only preliminaries to the work of the following years, which culminated in the synthesis, for the first time outside Germany, of arsephenamine * and later neoarsphenamine.*

The development of Salvarsan by Ehrlich and Hata had created not only a revolution in the treatment of syphilis (6, 7) but also had

* Salvarsan, 606, Arsenobenzol, Diarsenol and Arsphenamine all apply to the product 3,3′-Diamino-4,4′-dehydroxyarsenobenzene dihydrochloride. Neosalvarsan, 914, Novarsenobenzol, Neodiarsenol and Neoarsphenamine are all designations for the compound sodium 3,3′-diamino-4,4′-dihydroxyarsenobenzene-N-monomethylenesulfoxylate.

opened a new vista of chemotherapeutics. This drug and its near-relative, Neosalvarsan, quickly demonstrated their effectiveness in the treatment of syphilis and were in great demand in this country. Yet, because of existing patents, they were available only by importation from Germany. The sole distributor of German Salvarsan in the United States was Farbwerke-Hoechst Company, which represented the manufacturers, Lucius and Bruning of Hoechst am Main, Germany. In 1914, before the outbreak of World War I in Europe, American physicians paid about $3.50 for an 0.6 gm. ampule of Salvarsan. As the war progressed, shipments from Germany became fewer and then were stopped entirely by the British naval blockade. The price of Salvarsan soared rapidly to $10.00 to $35.00 per ampul, black-marketing occurred, and dangerous and worthless imitations appeared on the market. Other scarce drugs included, just to mention a few, Atophan (cinchophen), Pyramidon (aminopyrine), Aspirin (acetyl-salicylic acid) and Phenacetin (acetophenetidin), the latter setting the record of all chemical price advances, rising from 84 cents to 42 dollars a pound (8).

Fortunately, the emergency having been foreseen in the early days of the war by the founders of the Dermatological Research Laboratories (D. R. L.), the difficult and complex synthesis of arsphenamine was solved in the spring of 1915. By the end of the year the new product had been evaluated in the treatment of syphilitic patients at the Polyclinic (9).

But while it was now possible to produce arsphenamine in the laboratory and offer it at less than half of prevailing prices, there was no legal way of marketing it as long as the German firm enjoyed an absolute and unchallenged monopoly. The outcry to free this country from German domination in the field of synthetic drugs now became a keen struggle to overcome the stranglehold which the German chemical industry was exerting on the American consumer by virtue of the existing patents. Public opinion clamored for the abrogation of the German patents. Typical of that trend are the following excerpts from an editorial which appeared in the Journal of the American Medical Association (10) immediately following the entry of the United States into the war.

"The Journal believes that this patent should be abrogated, not alone because the patentees have not supplied the demand, not alone because they have dictated to the medical profession who should have the drug and how much a physician might have, not alone because

of the war with Germany, not alone because of the special needs of the government at this time for the control of venereal diseases, not alone because, as some claim the patent at Washington does not correctly describe the product, but also because the people who are supplying this product are charging prices that are exorbitant compared to the price of which others in this country can supply it. . . . While we are emphasizing here the cost, there is after all a greater question, and that is the supply necessary to help control the ravages of one of the most serious diseases which afflict humanity today. It is the duty of Congress to abrogate the patent on this preparation and, incidentally, on all medicinal preparations of importance."

The federal government did take action. In October, 1917, the Adamson Bill, known as the "Trading with the Enemy Act" became law. Under this act the Federal Trade Commission was granted authority to issue licenses to responsible American citizens to operate patents owned by enemy aliens. In November, 1917, License Number 1 was issued to the Dermatological Research Laboratories to manufacture arsphenamine (Arsenobenzol) (11). In March, 1918, the D. R. L. and three other Laboratories were licensed to manufacture neoarsphenamine (12).

There were both immediate and long-range effects of the Trading with the Enemy Act. The immediate effect was to provide the American fighting forces and the American people with needed drugs and chemicals. But even more important, this Act freed the American pharmaceutical and chemical industries from German domination and fostered their growth. The pioneer scientific workers during this period not only liberated American chemical research and the American chemical industry in their own day, but also helped to create the American technical genius of today (8, 13, 14, 15).

The American synthetic chemical and drug industry of today is deeply indebted to the undaunted, enterprising and pioneering spirit of the little band of scientists of a generation ago. They spearheaded the movement to liberate American chemical industry and their successful accomplishments mark the emergence of America as the leader in the manufacture of synthetic drugs. Their spirit may well serve as an inspiration in the keen world struggle which is being waged in our own time (16).

BIBLIOGRAPHY

(1) New and Nonofficial Remedies 1916, A. M. A. Chicago, 1916.

(2) The Future and Progress of American Medicine in the Age of Chemistry, pp. 58 and 65, Chemical Foundation, Inc., New York, 1921.

(3) Kolmer, J. A., History of the Research Institute of Cutaneous Medicine in History of Dermatology in Philadelphia, by Reuben Friedman, Froben Press, Inc., Fort Pierce Beach, 1955.

(4) Schamberg, J. F., Kolmer, J. A., Ringer, A. I. and Raiziss, G. W., Studies in Psoriasis, J. Cutaneous Medicine, Oct.-Nov., 1913.

(5) Schamberg, J. F., Kolmer, J. A. and Raiziss, G. W., Mercurophen, *J. Infectious Diseases, 24:*347 (1919).

(6) Ehrlich and Hata, Die Experimentelle Chemotherapie der Spirilossen, Springer, Berlin, 1910.

(7) Ehrlich and Bertheim, Uber das Salzsaure-3-3' Diamino-4-4' dioxyarsenobenzol und seine Nächsten Verwandten, *Berichte der Deutschen Chemischen Gesellschaft, 45:*756 (1912).

(8) Haynes, William, American Chemical Industry, Vol. 3, p. 318, D. Van Nostrand, New York, 1945.

(9) Schamberg, J. F., Kolmer, J. A. and Raiziss, G. W., Summary of Chemotherapeutic Studies in Experimental Trypansomiasis, *J. A. M. A., 64:*2142 (1915).

(10) Abrogate the Patent on Salvarsan, editorial, *J. A. M. A., 68:*1187 (1917).

(11) *U. S. Public Health Reports, 32,* 2071 (1917).

(12) *U. S. Public Health Reoprts, 33:*540 (1918).

(13) Haynes, Willia, American Chemical Industry, 6 volumes, D. Van Nostrand, New York, 1945. Vols. 2 and 3 contain numerous references on this development.

(14) The Philadelphia Record, March 3, 1921.

(15) Resolutions Council of the American Dermatological Association, *J. Cutaneous Diseases, 34:*632 (1916).

(16) Lichtin, A. and Schamberg, I. L., Jay Frank Schamberg, *J. A. M. A., 73:*493 (1956).

DRUG INFORMATION SOURCES*

Brazil and Cuba

BRAZIL

Vademecum Médico-Farmacêutico. 4th ed. São Paulo, Livraria Vademecum Editôra, 1952. 946 pp.

Part I is an alphabetic list of pharmaceutical specialties and preparations marketed in Brazil. Information given for individual preparations includes name of manufacturer, composition in detail, actions, indications, dosage, administration, forms and packing. Part II is a therapeutic index to the drugs in Part I. Part IV is a list of manufacturers, representatives, distributors and importers of pharmaceutical preparations with their addresses. Part III lists mineral springs and rest homes. The 4th edition is currently out of print, but a 5th edition is in process. Publisher's address: Rua Barão de Itapetininga, 273, 7° andar, São Paulo.

Formulário Médico-Farmacêutico Brasileiro, by Virgílio Lucas. Rio de Janeiro, 1953. 660 pp.

An alphabetic list of medical-pharmaceutical formulas, giving composition, method of preparation, action, indications and dosage. General information useful for doctors and pharmacists is included in the form of tables, e.g., solubility data, antidotes for poisons, specific gravity cómparisons, etc. Published by the author.

Dicionário de Sinônimos (Químicos-Farmacêuticos), by Virgílio Lucas. 5th ed. Rio de Janeiro, Editôra Cientifica, 1956. 787 pp.

An extensive list of technical, commercial and popular names and synonyms for chemical products and substances, plants and pharmaceutical preparations, including the most important medicaments used in homeopathy.

---

*A World List; compiled by the Pharmaceutical Section, Science-Technology Division, Special Libraries Association.

Dicionário de Sinônimos Químico-Farmacêuticos, by Dr. Mario Rangel. 2d ed. Rio de Janeiro, Irmãos Di Giorgio & Cia., 1954. 246 pp.

This dictionary includes pharmaceutical, medicinal and biological terms, reactions and formulas known by personal names, as well as drugs, chemicals and medicinal plants. Publisher's address: Rua Canindé, 32, Rio de Janeiro.

Dicionário Brasileiro de Plantas Medicinais, by Meira Penna. 3d ed. Rio de Janeiro, Livraria Kosmos, 1946.

A dictionary of medicinal plants indigenous to the climate of Brazil. Plants are entered by botanic name with brief entry providing name of family, alternate names, habitat, botanic characteristics and medicinal uses. Publisher's address: Rua do Rosario, 137, Rio de Janeiro and Rua Marconi, 91-93, São Paulo.

Livro de Precos Drogasil. São Paulo, Drogasil Inc. 626 pp.

A complete alphabetic price list of drug specialties, dietetic products, homeopathic products, plant drugs, biologicals and sundries sold in Brazil, published by the retail-wholesale drug organization "Drogasil". It is a sort of stock file to be used by the sales clerk at the sales counter, listing name, pharmaceutical form, dosage amount or concentration of the chief ingredient, package form and price of each drug. New drugs, new forms, price changes, etc., appear periodically in mimeographed lists. Ample space is provided in the printed text for additions and corrections. The book sells for about $15 in U. S. currency. Publisher's address: Rua Santo Amaro, 554, São Paulo.

CUBA

Asociación Farmacéutica Nacional. **Formulario Nacional.** 2d ed. Havana, Imprenta de La Universidad de La Habana, 1950. 195 pp.

The official Cuban formulary.

Servicios Médicos Psico-Pedagógicos y Publicitarios S.A. **G.T.D.C.; Guia Terapeutico de Cuba; Suplemento de Archivos Medicos de Cuba.** Havana, Impresora "Múltiple". Free.

Monographs include formula, dose and form of products arranged under the manufacturer's name. Alphabetic product and therapeutic indexes are included. Revised every three months. Publisher's address: Presidente Zayas #206, Havana.

* * *

A limited number of reprints are available for distribution by the Committee at 30¢ each. Requests should be sent to Miss Elinor Piro, Assistant Librarian, Winthrop Laboratories, 1450 Broadway, New York 18, N. Y.

The Committee on Drug Information Sources has the following members:

Anne McCann, Chairman; Elizabeth Boykin, Harold Oatfield, James L. Olsen, Jr., Maxine Painter, Elinor Piro, Clara Robeson, Walter Southern, Irene Strieby and Charlotte Studer.

SELECTED ABSTRACTS

Neomycin in the Treatment of Hepatic Cirrhosis. Fisher, C. J., and Faloon, W. W. *New England J. Med. 256:*1030 (1957). The oral administration of neomycin proved to be an effective agent in controlling the ammonia intoxication associated with hepatic cirrhosis. Daily oral doses of 8 to 12 Gm. of neomycin were given to 11 patients in a series of 12 trials. In all cases, the high blood levels of ammonia were reduced to normal. No difference in the effect on the ammonia level was noted with the dosages employed. In the three patients where present, neurologic manifestations of stupor or confusion cleared 24 to 48 hours after the blood level of ammonia was reduced. The blood levels of ammonia rose again to the original levels following the withdrawal of neomycin. In most cases this rise was prompt but in one patient it was prolonged to about 2 months.

Stool cultures were performed on all of the patients. These cultures were sterile or yielded only yeast after therapy with the 12 Gm. dosage, but a clostridium was also found in two patients receiving the 8 Gm. dosage.

All of the patients in this study had a long history of excessive alcohol ingestion, usually associated with a poor dietary intake.

The authors concluded that neomycin reduced the blood ammonia in these patients because of its effect on the bacterial flora of the intestine. It was felt that the antibiotic had little effect on the ammonia already in the blood.

The Treatment of Vaginitis With Hydrocortisone Tablets. Lang, W. R. *Postgrad. Med. 21:*320 (1957). Hydrocortisone has been employed topically in the form of creams and lotions for the treatment of anogenital pruritus. It has also been recommended for use in tablet form for the local treatment of vaginitis. The author investigated the value of the steroid in the latter form in a series of 78 patients. Forty-four patients had a diagnosis of nonspecific vaginitis, 22 of atrophic, 5 of trichomonal, and 7 of candidal vaginitis.

The patients were instructed to insert one or, in a few instances, two vaginal tablets high in the vaginal vault each evening before retiring for a period of 10 days, except in the cases of atrophic vaginitis in which treatment was for 3 weeks. The tablets employed contained 10 mg. of hydrocortisone free alcohol in a Carbowax base with 1 per cent magnesium stearate and 2 per cent glyceryl monostearate. No other vaginal therapy was permitted, including douching.

Of the patients with nonspecific vaginitis, about one-fifth noted a decrease in discharge and about one-third of the 27 patients with pruritus obtained relief. Redness of the vaginal vault was observed to lessen but there was no decrease in the number of leukocytes.

Of the patients with atrophic vaginitis, 8 of 10 women obtained relief from pruritus and discharge was lessened in 12 of 18. In the patients wtih trichomonal and candidal infections, there was some relief from itching but no evidence of any influence on the infectious agents.

The author concluded that hydrocortisone vaginal tablets have merit in providing symptomatic treatment of vaginitis, probably because of the general anti-inflammatory properties of the steroid. However, since the steroid is capable of being absorbed from the vagina, it should be used only as a temporary measure and in moderate dosage.

The Use of Enzyme Preparations in Certain Gynecologic Conditions. Hunter, R. G., Henry, G. W., Heinicke, R. M., and Civin, W. H. *Am. J. Obst. and Gynecol. 73:867* (1957). Preparations of two proteolytic enzymes, papain and bromelain, showed promise in the management of certain gynecologic conditions. Papain is obtained from the green fruit of the papaya tree and bromelain is obtained from the stems of pineapples.

The intravaginal instillation of these enzymes caused the thick, tenacious mucus so often seen in the cervical canal to dissolve. When used prior to a salpinogram, the anatomy of the cervical canal could be easily and accurately visualized. Lesions and inflammatory changes in the canal could be diagnosed with increased accuracy.

During these studies it was noted that the cervical canal was greatly dilated and relaxed. Therefore, instillations of the enzymes were given to 64 patients with severe dysmenorrhea. Bromelain was found to be more satisfactory than papain because it was practically

odorless while papain had a disagreeable odor and its solutions were more stable than those of papain.

Immediate relief from these instillations was obtained in 40 patients. The remaining 24 had poor or fair results. Best results were obtained in teen-agers, young nulliparas, and a few older patients without concurrent gynecologic disease.

The authors also found that the enzymes were useful for diagnosing a physiologically incompetent internal cervical os, which may be responsible for the occurrence of habitual abortion. Dilitation induced by these enzymes is apparently a specific means of demonstrating this conditon. However, the authors did not determine whether repair of the defect, once diagnosed, will enable future pregnancies to be carried to term.

The Use of Silicones in Dermatologic Conditions. LeVan, P., Sternberg, T. H., and Newcomer, V. D. *Am. Assoc. of Indust. Nurses Jour. 5*:28 (1957). Once dermatitis of the hands is established, an endless variety of physical, bacterial and chemical agents can maintain the process despite the removal of the original offending agents. In addition, pathologic changes frequently develop. Consequently, control of dermatoses is essential.

The authors presented a formula and described the benefits from the use of a lotion found to be useful in the control of dermatoses, as well as cosmetically acceptable. The lotion contained 1.5 per cent silicone (Dow-Corning 200 or 555), 0.2 per cent glyoxyl diureide, 0.1 per cent camphor, 0.1 per cent menthol, and 0.25 per cent hexachlorophene in an ethanolamine stearate base.

Preliminary investigation of the lotion in laboratory animals consisted of topical applications for 21 days, vaginal instillations for a similar period, intracutaneous sensitization tests and instillations into the eyes. None of these tests revealed evidence of significant irritative effects. Sensitivity could not be produced after a series of intracutaneous injections repeated after a rest period.

The largest group of patients treated with the lotion were those with housewive's eczema, often called "dishpan hands". There were 109 subjects in this group, of which 95 experienced complete healing while only one subject had no healing. In some patients with extreme dryness, only slight improvement was noted until an emollient cream

was prescribed to be used nightly. Thirty-eight additional subjects had contact dermatitis other than housewive's eczema. Even though they continued at work, and thus with continuing exposure, 26 patients showed complete healing following use of the lotion.

Diaper rash in 31 infants showed healing in 20 cases. Angular stomatitis, cheilitis and/or saliva eczema responded in 11 of 14 patients. Another group of six patients with follicular hyperkeratosis or hyperkeratotic dermatoses showed complete or partial healing in all six patients.

The authors indicated that one of the most striking effects from the use of the lotion was the rapidity with which hyperkeratinization, as evidenced by roughness, scaling, and thickening, disappeared.

Therapy With Cortisone in Active Rheumatic Carditis. Gibson, H. C. *U. S. Armed Forces Med. J. 8:*1405 (1957). The treatment of 35 adults and 3 children with active rheumatic carditis was started early and consisted of prolonged bed rest, chemotherapeutic drugs, and high doses of cortisone. Treatment with cortisone was started with daily oral doses of 300 to 400 mg., given in divided doses every 6 hours. This dosage was continued until the patient was asymptomatic and the sedimentation rate, C-reactive protein, and electrocardiogram had returned to normal. This was usually 7 to 10 days. Then an attempt was made to reduce the dose by 50 mg. every 4 to 7 days to a daily dose of 200 to 300 mg. After 6 to 8 weeks of treatment, provided all findings indicated a likely cessation of activity, the dosage was decreased by 25 to 50 mg. a day at 3- to 4-day intervals to zero.

Cortisone suppressed positive signs of activity throughout the active period of the disease in all but 2 of the 38 patients treated. Twenty-three patients were left with no demonstrable heart damage. Significant murmurs had been present in 33 patients but these disappeared in 19 of the patients.

The author emphasized the importance of an early beginning of steroid therapy, that it be given in fully suppressive doses, and that it not be discontinued too early or given in courses. He indicated that he was convinced that the progression of valvular damage in cases of active rheumatic carditis ceased when inflammation was suppressed by adequate cortisone therapy.

An Evaluation of Sulfaethylthiadiazole in Sustained Release Forms. Sablosky, L. *Antibiot. Med. & Clin. Ther. 4:729* (1957). Sulfaethylthiadiazole (SETD) has been found to have a wide range of antibacterial activity against both Gram-positive and Gram-negative microorganisms. When administered orally, it is absorbed rapidly and is also excreted rapidly (nearly 100 per cent within 72 hours). Only about 10 per cent of the drug is acetylated in the body. To take better advantage of these properties, the drug was prepared in a liquid and in tablets in sustained release form. The design of the dosage form was to provide a slow release of the drug over a prolonged period of time so that therapeutic blood levels could be maintained.

SETD was given to most adult patients initially in a dose of 4.0 Gm., whether the sustained release liquid or the sustained release tablets were employed. After the first dose, 2.0 Gm. were given every 12 hours. Generally the duration of treatment varied from 3 to 5 days.

A total of 168 patients with various infections were treated. Results were considered "good" when all symptoms disappeared and the infected areas cleared or were markedly improved. Good results were obtained in 85 per cent of the 109 patients treated with the liquid formulation and in 88 per cent of the 59 patients treated with the tablet. Most patients were afebrile within 12 to 24 hours after taking the first dose of SETD in sustained release form. In patients with urinary tract infections, because of the high incidence of recurrences, therapy was usually continued for 8 hours. The types of infections treated included: respiratory infections, otitis media, lymphadenitis, gastrointestinal infections, urinary tract infections, and a skin infection.

None of the patients reported serious side effects such as crystalluria, renal blockage, or hematuria. Minor side effects were reported in ten patients, such as, nausea and vomiting, skin reactions, and urinary frequency. Most of these reactions were in children or infants.

Blood level studies were conducted in 9 persons following a single 4.0 Gm. dose of SETD in sustained release tablet form. The results indicated that the average blood level was within the therapeutic range during 12 hours after administration.

BOOK REVIEWS

Subsidia Pharmaceutica I. (S. Ph. I.) Editors: Scientific Center of the Swiss Pharmaceutical Society (Wissenschaftliche Zentralstelle des Schweizerischen Apotheker-Vereins). Publishers: Swiss Pharmaceutical Society (Selbstverlag des Schweizerischen Apotheker-Vereins). 220 pp. Zürich, 1957. Price: 45 Swiss Francs (approx. $11.00).

This compendium is published for the benefit of the practicing pharmacist to familiarize him with new titles, new products, new chemicals, and new methods. These changes occur so frequently that it is an almost unsurmountable task to keep posted. This publication is in the form of a loose-leaf ringbinder which makes it very flexible in usage, allowing for easy changes and additions. Provision is also made for inserting personal notes and information by having included a set of blank papers.

The book is divided into several chapters. The first chapter: "Index Nominum Rerum Pharmaceuticarum" (listing of pharmaceuticals) gives an alphabetical order all "Denominations Communes Internationals—DCI" (International General Titles) which are recommended by the World Health Organization and which are used in the scientific literature and in prescriptions. Besides their general titles, their corresponding titles as listed in several pharmacopeias are given, such as: Ph. Int. I, Ph. Helv. V, Ph. Gall. VII, B. P. 1953, Ph. Dan. 1948, U. S. P. XV, etc. Furthermore, the authors cite some trade-mark names of certain specialities. Naturally, this had to be restricted to preparations where the active ingredient is the drug prescribed and not a mixture or combination of drugs. With this approach, the authors hope to familiarize the pharmacist with the titles used in different countries and, at the same time, to stress the international titles which are currently used.

The second chapter: "Therapeutische Stoffklassen" (pharmacological classification) attempts to instruct the pharmacist in certain fields of pharmacologic action of medicaments. So far, only the autonomic nervous system has been discussed. The authors will continue to publish other chapters in this very important field of pharmacological action.

It is a well-written chapter supplemented by drawings of several schemes such as the autonomic nervous system, its innervation, the anatomic location of the ganglia, and the chemical transmission of impulses in the autonomic nervous system. Furthermore, tables summarize the effect of stimulation on the different organs. This is followed by a discussion of various medicaments including some proprietaries.

The remaining chapters of this compendium are of a more technical nature such as: Analytical Methods, New Galenical Preparations (not official), a Commentary on "Prescriptiones Magistrales" (a Swiss prescription formulary), and Equipment and Apparatus for manufacturing on a small scale.

The authors are to be complimented on an enterprise well executed. The format is very convenient, the printing is very clear, the drawings are excellent, and the arrangement facilitates easy handling. This first publication will be followed as quickly as possible by others according to a well established plan. It thus serves as an aid to the pharmacist for quick reference and information. By publishing such a compendium and keeping it up to date, the Swiss Pharmaceutical Association is rendering a great service to its membership.

ELSA EHRENSTEIN

Vogel-Knobloch: Chemie und Technik der Vitamine, Third Edition, 2nd Volume "The Water-Soluble Vitamins", 2nd part, 2nd installment, pp. 161-320. Publisher: Ferdinant Enke Verlag, Stuttgart, Germany, 1957. Paperbound; DM. 28.80 (approx. $7.25).

The second part of the second volume of *Chemie und Technik der Vitamine* continues with the discussion of water-soluble vitamins. It is published in four different installments.

The second installment (pp. 161-320) concludes the discussion of Nicontinic Acid Amide and continues with Pyridoxine (Vitamin B_6). For each vitamin, the author lists the history, source, chemical constitution, synthesis, properties, analytical data, etc. As in Part I, excellent literature references make this book very valuable.

The two remaining installments will cover other vitamins of the B-complex, as well as vitamins C and P.

ELSA EHRENSTEIN

SCHERING

Fine Pharmaceuticals

products of
original Schering research

METICORTEN®	METICORTELONE®
CHLOR-TRIMETON®	CORICIDIN®
NEORAVAL®	TRILAFON®
METI-DERM®	METRETON®
METIMYD®	PRANTAL®

American Journal of Pharmacy

The American Journal of Pharmacy is the oldest continuously published scientific periodical of its kind in America, having been established by the Philadelphia College of Pharmacy in 1825. After the original issue there were three other preliminary numbers until 1829, when regular publication began. From then until 1852 four issues were published annually, with the single exception of 1847, when an additional number appeared. Six issues a year were printed from 1853 to 1870, at which time the Journal became a monthly publication.

Former Editors of the Journal have been: Daniel B. Smith, 1825-1828; Benjamin Ellis, 1829-1831; Robert E. Griffith, 1831-1836; Joseph Carson, 1836-1850; William Procter, Jr., 1850-1871; John M. Maisch, 1871-1893; Henry Trimble, 1893-1898; Henry Kraemer, 1898-1917; George M. Beringer, 1917-1921, and Ivor Griffith, 1921-1941.

Established and maintained as a record of the progress of pharmacy and the allied sciences, the Journal's contents and policies are governed by an Editor and a Committee on Publications elected by the members of the College.

Manuscripts should be sent to the Editor, who does not assume any responsibility in connection with the views or investigations of contributors of accepted manuscripts, other than to exercise general care in selection.

Contributors are allowed a reasonable number of copies of this Journal, free of charge, if applied for when the proof is returned.

Reprints, if desired, should be ordered when the proof is returned. The table below shows the *approximate* cost of reprints, the make-up of the pages to be identically the same as in the Journal. The actual cost may vary from the figures given, and will depend upon the amount of presswork, paper, binding, and other factors. Reprints containing half-tones may be expected to cost somewhat more than the rates given.

	2 pp.	4 pp.	8 pp.	16 pp.	Covers with Titles
50 copies.....	$ 4.50	$10.00	$16.25	$27.50	50 copies..... $ 7.50
100 "	7.50	13.75	21.25	40.00	100 " 12.50
250 "	10.00	17.50	27.50	53.75	250 " 17.50
500 "	15.00	25.00	35.00	68.75	500 " 26.25

Your RED CROSS

is

on the job for YOU

Give it YOUR SUPPORT